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Clustering of Shaker-type K+ channels by interaction with a family of membrane-associated guanylate kinases.

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ANCHORING of ion channels at specific subcellular sites is critical for neuronal signalling, but the mechanisms underlying channel localization and clustering are largely unknown (reviewed in ref. 1). Voltage-gated K+ channels are concentrated in various neuronal domains, including presynaptic terminals, nodes of Ranvier and dendrites, where they regulate local membrane excitability. Here we present functional and biochemical evidence that cell-surface clustering of Shaker-subfamily K+ channels is mediated by the PSD-95 family of membrane-associated putative guanylate kinases, as a result of direct binding of the carboxy-terminal cytoplasmic tails to the K+ channel subunits to two PDZ (also known as GLGF or DHR) domains in the PSD-95 protein. The ability of PDZ domains to function as independent modules for protein-protein interaction, and their presence in other junction-associated molecules (such as ZO-1 (ref. 3) and syntrophin), suggest that PDZ-domain-containing polypeptides may be widely involved in the organization of proteins at sites of membrane specialization.

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1: Science. 1995 Sep 22;269(5231):1737-40. Related Articles, Links

Domain interaction between NMDA receptor subunits and the postsynaptic density protein PSD-95.

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The N-methyl-D-aspartate (NMDA) receptor subserves synaptic glutamate-induced transmission and plasticity in central neurons. The yeast two-hybrid system was used to show that the cytoplasmic tails of NMDA receptor subunits interact with a prominent postsynaptic density protein PSD-95. The second PDZ domain in PSD-95 binds to the seven-amino acid, COOH-terminal domain containing the terminal tSXV motif (where S is serine, X is any amino acid, and V is valine) common to NR2 subunits and certain NR1 splice forms. Transcripts encoding PSD-95 are expressed in a pattern similar to that of NMDA receptors, and the NR2B subunit co-localizes with PSD-95 in cultured rat hippocampal neurons. The interaction of these proteins may affect the plasticity of excitatory synapses.

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